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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/420,433	10/12/1999	DAVID SIDRANSKY	JHU1180-1	2810

7590 02/10/2003

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EXAMINER	
JOHANNSEN, DIANA B	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/420,433	SIDRANSKY, DAVID	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 7-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This action is in response to paper nos. 21 and 22, filed November 12, 2002. Claims 5-6 have been canceled, and claims 1-2, 12, 18-21 and 25 have been amended. Claims 1-4 and 7-27 are now pending and under consideration. The amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

3. Claims 1-4 and 7-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15-17, 23, and 27 are indefinite because it is unclear as to how the claims are intended to further limit the claims from which they depend. Claims 15-16 require that "said neoplastic nucleic acid is a mutated tumor suppressor gene," and claim 16 further requires that "said tumor suppressor gene is the p53 gene." Claim 17 requires that "said neoplastic nucleic acid is an oncogene," claim 23 recites that "the mutant target nucleic acid is selected from the group consisting of an oncogene and a tumor suppressor gene," and claim 27 requires that "said neoplastic nucleic acid is a mutated

tumor suppressor gene." It is noted that each of the claims from which instant claims 15-17, 23, and 27 depend has been amended in paper no. 21 to require one of a particular group of neoplastic/mutant nucleic acids, specifically, one of APC, DCC, NF1, NF2, RET, VHL and WT-1. It is further noted that it is well known to those of skill in the art that each of APC, DCC, NF1, NF2, RET, VHL and WT-1 is considered by those skilled in the art to be a "tumor suppressor." Thus, given the amendments to the independent claims, it is unclear as to how or whether claims 15-17, 23, and 27 are further limiting. For example, are the dependent claims intended to further limit the claims to a particular subset of the genes recited in the independent claims (and if so, what subset?), or are the dependent claims intended to improperly broaden the scope of the claims by allowing the claims to encompass oncogenes, to encompass any type of tumor suppressor, etc., as the language of the claims suggests? Further, the recitation of p53 in claim 16 is particularly unclear, as this recitation suggests either that applicant considers the recitation of APC, DCC, NF1, NF2, RET, VHL and WT-1 to encompass p53 (as would be necessary in order for the recitation of p53 to be further limiting), or that the dependent claims are not in fact further limiting of the claims from which they depend (as is required of a proper dependent claim). Clarification is required.

Claims 1-4 and 7-27 are indefinite over the recitation of the language "wherein the (mutant target/neoplastic/target neoplastic) nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1" in independent claims 1, 12, 18-20 and 25. As discussed in the paragraph immediately above, those of skill in the art would consider

each of APC, DCC, NF1, NF2, RET, VHL and WT-1 to be a particular "tumor suppressor," which particular tumor suppressors are known to the skilled artisan. However, several of applicant's dependent claims include recitations indicating that this recitation encompasses p53, as well as other tumor suppressors, and oncogenes (see paragraph immediately above). Accordingly, it is unclear as to how the recitation of the group of genes "APC, DCC, NF1, NF2, RET, VHL and WT-1" in the claims is intended to limit the claims. While it is apparent from applicant's claims (and particularly, dependent claims 15-17, 23 and 27) that applicant intends for these terms to have a meaning different from that known to one of skill, the manner in which applicant intends for this recitation to be limiting is unclear, as are the metes and bounds of the claims. Applicant is also reminded that while applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Clarification is required.

Claim Rejections - 35 USC § 102

4. In view of the cancellation of claims 5-6, the rejection of the claims under 35 U.S.C. 102(a) as being clearly anticipated by Nees et al (Cancer Research 53(18):4189-4196 [9/1993]) is moot.

5. Claims 1-4, 7-8, 10, 12, 14-16, and 18-19 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Nees et al (Cancer Research 53(18):4189-4196 [9/1993]), for the reasons set forth below and in the Office action of paper no. 19.

The response traverses the rejection on the grounds that "the claims as amended recite to specific mutant target nucleic acids and target neoplastic nucleic acids, none of which is p53" and that "Nees et al. do not teach or suggest a target nucleic acid other than p53." These arguments have been thoroughly considered but are not convincing for the following reasons. While it is acknowledged that applicant has amended independent claims 1, 12, and 18-19 to recite a particular group of nucleic acids, applicant's claims as written indicate that p53 is considered to be encompassed by this group. Specifically, while claim 12 does recites the limitation "the neoplastic nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1," claim 16, which is dependent on and further limiting of claim 12, is drawn to methods in which "said neoplastic nucleic acid" is "the p53 gene" (see claims 15-16). Further, several of applicant's dependent claims indicate that the instant claims are intended to be sufficiently broad so as to encompass nucleic acids other than those specifically recited in the independent claims, including both oncogenes and other tumor suppressors (see claims 15-17, 23, and 27, and see also paragraph 3, above). Accordingly, applicant's argument that the instant claims exclude p53 is not persuasive.

Nees et al teach all the limitations recited in present claims 1-4, 7-8, 10, 12, 14-16, and 18-19, and therefore this rejection is maintained.

6. Claim 13 is rejected under 35 U.S.C. 102(a) as being clearly anticipated by Nees et al (Cancer Research 53(18):4189-4196 [9/1993]), in light of the teachings of Sobol et al (U.S. Patent No. 5,543,296 [8/6/1996; effective filing date 6/26/1991]), for the reasons set forth below and in the Office action of paper no. 19.

First, the response traverses the rejection on the grounds that Nees et al "does not teach or suggest a target nucleic acid as recited in the claims." This argument has been thoroughly considered but is not convincing for the same reasons set forth in paragraph 5, above. Second, the response argues that Sobol et al do not teach the target nucleic acids required by the claims. However, the Sobol et al reference was not cited for a teaching of particular target nucleic acids, but rather was cited merely for its teachings regarding the sensitivity of PCR (see paragraph 6 of the Office action of paper no. 19). As discussed above in paragraph 5 and in paper no. 19, Nees et al teach target nucleic acids meeting the requirements of the instant claim as written. Accordingly, applicant's arguments are not persuasive.

Nees et al teach all the limitations recited in present claim 13, and therefore this rejection is maintained.

Claim Rejections - 35 USC § 103

7. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nees et al (Cancer Research 53(18):4189-4196 [9/1993]) in view of Watling et al (Head and Neck 14;437-444 [11-12/1992]), for the reasons set forth below and in the Office action of paper no. 19.

First, the response traverses the rejection on the grounds that "previously pending claim 9, which included p53 as a target nucleic acid, was directed to detecting a mutant target p53 as an indication of a benign neoplasm," whereas "Watling et al. teach away from such a method because the reference teaches that p53 is not over-expressed in benign neoplasms." This argument has been thoroughly considered but is not persuasive. The instant claim did and does not require, e.g., that detection of p53 over-expression be indicative of the presence of a benign neoplasm. Rather, the claim is sufficiently broad so as to encompass detection of p53 in any manner (including that suggested by Nees et al in view of Watling et al, as set forth in the Office action of paper no. 19) so as to permit detection of a benign neoplasm. Second, the response traverses the rejection on the grounds that Watling et al "do not teach or suggest a target nucleic acid as recited in the claims," and thus that "Watling et al. do not provide the teaching missing in the Nees et al. reference." However, the Watling et al reference was not cited for a teaching of particular target nucleic acids, but rather was cited for its teachings regarding the relative levels of p53 expression in malignant and benign head and neck tumors (see paragraph 7 of the Office action of paper no. 19). As discussed above in paragraph 5 and in paper no. 19, Nees et al teach target nucleic acids meeting the requirements of the instant claim as written. Accordingly, applicant's arguments are not persuasive.

The combined references of Nees et al and Watling et al suggest all the limitations of present claim 9, and therefore this rejection is maintained.

8. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nees et al (Cancer Research 53(18):4189-4196 [9/1993]) in view of Mullis et al (U.S. Patent No. 4,683,195 [7/28/1987]), for the reasons set forth below and in the Office action of paper no. 19.

The response traverses the rejection on the grounds that neither Nees et al nor Mullis et al teach or suggest target nucleic acids encompassed by the claim. However, as discussed above in paragraph 5 and in paper no. 19, Nees et al teach target nucleic acids meeting the requirements of the instant claim as written. Further, the Mullis et al reference was cited not for a teaching of a target nucleic acid, but for its teachings regarding the cloning of amplification products (see paragraph 8 of paper no. 19). Accordingly, applicant's arguments are not persuasive.

The combined references of Nees et al and Mullis et al suggest all the limitations of present claim 11, and therefore this rejection is maintained.

9. Claims 20-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nees et al (Cancer Research 53(18):4189-4196 [9/1993]) in view of Sobol et al (U.S. Patent No. 5,543,296 [8/6/1996; effective filing date 6/26/1991]), for the reasons set forth below and in the Office action of paper no. 19.

The response traverses the rejection on the grounds that neither Nees et al nor Sobol et al teach or suggest target nucleic acids encompassed by the claims. However, as discussed above in paragraph 5 and in paper no. 19, Nees et al teach target nucleic acids meeting the requirements of the instant claim as written. Further, the Sobol et al was cited not for a teaching of a target nucleic acid, but for its teachings regarding

nucleic acid extraction and detection of cancer-associated nucleic acids in lymph nodes (see paragraph 9 of paper no. 19). Accordingly, applicant's arguments are not persuasive.

The combined references of Nees et al and Sobol et al suggest all the limitations of present claims 20-27, and therefore this rejection is maintained.

10. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nees et al (Cancer Research 53(18):4189-4196 [9/1993]) in view of Knudson (Archives of Otolaryngology – Head and Neck Surgery 119(7):735-7 [7/1993]), for the reasons set forth below and in the Office action of paper no. 19.

The response traverses the rejection on the grounds that neither Nees et al nor Knudson et al teach or suggest target nucleic acids encompassed by the claims. This argument is not persuasive. Instant claim 17 as written requires that "said neoplastic nucleic acid is an oncogene." As discussed in paragraph 10 of paper no. 19, the Knudson et al reference teaches mutated forms of *ras*, which is an oncogene. Accordingly, applicant's argument is not persuasive.

The combined references of Nees et al and Knudson et al suggest all the limitations of present claim 17, and therefore this rejection is maintained.

Terminal Disclaimer

11. The terminal disclaimer filed on November 12, 2002, paper no. 22, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 6,025,127 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/872-9306 for regular communications and 703/872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Carla Myers

CARLA J. MYERS
PRIMARY EXAMINER

Diana B. Johannsen
February 4, 2003